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DETERMINANTS OF SURVIVAL IN LOW BIRTH WEIGHT INFANTS AT A TERTIARY HEALTHCARE FACILITY IN THE SOUTH EASTERN NIGERIA

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ABSTRACT

Low birth weight (LBW) babies account for a large number of neonatal deaths globally, with over 90% of these occurring in developing countries with low resources. Identifying factors that determine survival in these sub-groups of babies in such a low-resource setting will help clinicians prioritize care and improve outcomes. This study aims to bridge some knowledge gaps in this regard. This was a 45-month prospective study carried out at the Enugu State University Teaching Hospital (ESUTH), Enugu, Nigeria. All eligible newborns weighing between 500g and <2500g that were seen in this period were enrolled and monitored. Data collected were analysed with SPSS Version 24, and significant associations identified using logistic regression models. A total of 166 LBW neonates were enrolled, and 68.2% of them survived. Asphyxia and episodes recurrent apnoea were recorded at least once in 78.8% and 68.4% of the babies respectively, with about two-thirds requiring respiratory support at one time or the other. Survival in these LBW newborns was negatively associated with gestational age at birth of less than 32 weeks (OR 0.17; CI 0.03-0.50; P<0.01) as well as with episodes of recurrent apnoea (OR 0.07; CI 0.02-0.34; P<0.01). However, intra-uterine exposure to malaria was associated with a 15 times higher likelihood of survival (OR 15.41; CI 2.22-106.91; P=0.01). No significant associations was found between survival and attendances to antenatal care, mode of delivery, birth weight and a number of neonatal morbidities like necrotizing enterocolitis, hypothermia, hypoglycaemia, septicaemia, anaemia and neonatal jaundice. Survival rate among low birth weight neonates in a low resource setting is decreased with delivery at less than 32 weeks completed gestation as well as recurrent episodes of apnoea, but is increased with in-utero exposure to malaria.

Keywords: Newborns, Low birth weight, Survival, Enugu.

INTRODUCTION

Infants weighing less than 2500g, at birth irrespective of gestational age, are generally described as Low Birth Weights Hema and Johanson, (2000). This is further classified as very low birth weight (VLBW) if the birth weight lies between 1000g and less than 1500g, or Extreme Low Birth Weight (ELBW) if less than 1000g.The reason for Low Birth Weight include either Preterm births or born too Small for Gestational Age (SGA) Stoll and Kliegman, (2004). The global prevalence of LBW is 15.5%, which amounts to about 20 million LBW infants born each year, with 96.5% of them in developing countries (World Health Organization, 2006). Each year in Nigeria, about 5-6 million children are born LBW (Olu, 2005). There are several complications associated with LBW, these include, but are not limited to infections, hypoglycemia, hypothermia, jaundice, perinatal asphyxia and neurological sequelae like poor attention span Chan, 1994; Badshah et al. (2008). It is therefore, a major cause of death in the newborn, contributing to 60-80% of neonatal deaths (World Health Organization, 2006). Survival rates of LBW especially those of VLBW category, ranges from 43% in developing countries like Jamaica Trotman and Bell Y, (2006), to more than 90% in developed countries like the Netherlands Sabine et al. (2004). Several studies in developed countries have reported factors that determined survival of LBW babies especially those in VLBW and ELBW categories. Such factors include lower birth weight or gestational age, gender, no antenatal steroid, one minute Apgar, no spontaneous respiration in delivery room, body temperature/pH on admission, delivery in a tertiary center De Vonderweid Carta et al. (1991); Grupo, (2002); Vakrilova, (2002). To the Authors knowledge, very few of such study exist in developing countries. A study in India particularly included neonatal septicemia as a factor associated with survival in the VLBW babies. The current study was designed to show the factors that determine survival of this vulnerable group as seen a public health facility in Nigeria. Findings will hopefully be utilized to prioritize cares in their management.

MATERIAL AND METHODS

Study area

This is a prospective and analytical study carried out at the Special Care Baby Unit of Enugu State University Teaching Hospital (ESUTH) Enugu, from January 2013 to October 2016. ESUTH is a state-owned tertiary health facility. The Special Care Baby Unit is the arm of the Paediatric Department of the hospital which offers care to sick newborns within their first 28 days of life. It has two separate sections, the Out-born babies section for babies born outside the hospital, and the in-born section for babies delivered inside the hospital. Each section has 9 baby cots, 3 infant incubators, one Infant Resuscitaire (Open Incubator) among other accessories for neonatal care. The unit is managed by Consultant Neonatologists, Resident doctors and Paediatric Nurses

Enrolment of subjects

Babies born within or outside the hospital whose birth weight ranges from 500g to less than 2500g, and whose mothers or care givers gave informed written consent for the study were consecutively enrolled. Infants weighing below 500g at birth and those whose parents refused consent were excluded from the study. Prior to enrolment of the subjects, written informed consent was obtained from the parents. The aim of the study was communicated to the parents, and they were informed that participation is voluntary as well as withdrawal at any stage of the study. They were also informed that their refusal or agreement to participate do not in any way influence the cares offered to their babies while on admission.

Measures

Babies presenting within 24hours of birth were weighed naked twice with two different infant weighing scale (Kin-lee electronic infant weighing scale, model= EBSL-20 with maximum capacity= 20 kg & minimum of 100g and the Manual paediatric scale, model= ATZ-10 with maximum capacity= 10kg minimum capacity= 500g) read by different readers. Infants presenting after 72 hours of life were excluded from analysis. The birth weight is categorized into <1000g (Extreme Low Birth Weight), ≥ 1000g to <1500g (Very Low Birth Weight) and ≥ 1500 to < 2500g (Low Birth Weight). For those who met the inclusion criteria, the following information were obtained from the mother or care giver with a structured questionnaire administer by trained research assistants;

i. Gestational age at birth in weeks from the mother's Last Menstrual Period (LMP). Where the latter is not available, the gestational age is estimated using the New Ballard Scoring system by a neonatologist or a trained assessor. The gestational age is subsequently categorized into <32 weeks (Early Preterm), ≥ 32weeks to <37weeks (Late Preterm) and ≥37 weeks (Term)

ii. Place of birth; categorized into Inborn (born within the hospital) and Out-born (born outside the hospital)

iii. Attendance to Antenatal Care (ANC) by the mother categorized into 'YES' (if mother ever booked for and attended at least one session of ANC prior to delivery) and 'NO' if mother never booked or attended ANC for index baby.

iv. Mode of delivery; classified into spontaneous vaginal delivery with or without assistance (i.e. instrumentation) and operative delivery.

v. The baby's size for age is classified into those appropriate for gestational age (i.e. weight and/or occipito-frontal circumference and/or length lie within 10^{th} -

90th percentile for age) and small for gestational age (i.e. for weight and/or occipito-frontal circumference and/or length lie < 10th percentile for age).

vi. The gender, as depicted by the appearance of the external genitalia was documented as male or female.

vii. Asphyxia was measured using APGAR scoring system. The APGAR is an acronym for Appearance, Pulse rate, Grimace, Activity, Respiratory rate with two points awarded for each parameter. A maximum and minimum of 10 and 0 respectively is obtainable depending on the severity of oxygen deprivation to the newborn prior to delivery. The score is normally awarded at 1, 5, 10, 15 and 20 minutes after delivery. For this study, the APGAR score at 5 minutes was used. For babies presenting after the 5th minute, the 5-minute APGAR score in the referral note is used and where not documented, history obtained from the mother where applicable was used to estimate the APGAR score at 5 minutes. The scores were categorized into <7 or ≥ 7 for babies with and without asphyxia respectively.

Each baby is followed up with daily reviews by the medical team and when co-morbidities are identified, confirmation is made through history, clinical examination and laboratory investigations where necessary. Diagnosis was done by a neonatologist not involved in this study and where there were doubts about a diagnosis, second neonatologist was called in to confirm or refute the diagnosis. The outcome of each baby was categorized as 'survived' for discharged home alive or 'dead' where fatality occurred during the period of admission in the Special Care Baby Unit.

Data entry and analysis

The above measures were documented into a Microsoft Excel Sheet where data cleaning was done. Distribution of the measures of outcome and predictor variables were analyzed and recorded in percentages. Missing data were excluded from the analysis. The Chi-square and a 2-staged Binary Logistic Regression analysis were used to assess variables significantly associated with morbidity and mortality in newborn with low-birth weight. Data was analyzed using IBM® SPSS version 24.0.0 (SPSS Inc, Chicago, IL). Statistical significance was set at $P < 0.05$.

Ethical consideration

Ethical clearance was obtained from the Enugu State University Teaching Hospital Ethics Committee. Prior to recruitment of each subject, informed consent was obtained from every mother and newborn pair in their own right before recruitment. Participation in the study was entirely voluntary and no financial inducement whatsoever was involved. Participants were informed that voluntary withdrawal at any stage of interaction was guaranteed for them without any adverse effect for their babies. All information was handled with strict confidentiality.

RESULTS

A total of 166 LBW pre-term babies met the eligibility criteria, and were enrolled for this study. Table 1 summarizes the basic demographics of these babies. Of the total number, 86 (51.8%) were males, while the rest were females, and about two-thirds (68.2%) survived over this period.

Only 14.6% were born at term, while nearly half (47.6%) were delivered between 32 and 37 weeks gestation. The remainder was born before 32 weeks gestation. A slight majority of the deliveries were within ESUTH, and nearly nine out of every ten attended ante-natal care before delivery. As expected, all the babies were born with low weight, but about 1-in-3 had extremely low-birth weight (5.6%) and 23.8% very low-birth weight. The average weight was found to be 1.6kg (range of 0.5kg to 2.5kg), with about two-thirds being appropriate for their gestational ages. Just over 60% were born via spontaneous vaginal delivery with about 80% of the total participants recording normal APGAR scores of 7 or more in five minutes.

Variable	Parameters	Number	%
Gender	Male	86	51.8
(n 166)	Female	80	48.2
Outcome	Survived	107	68.2
(n 157)	Dead	50	31.8
Weight (k g)	≥1.5 to ≤2.5 (LBW)	113	70.6
(n 160)	≥1.0 to <1.5 (VLBW)	38	23.8
	<1.0 (ELBW)	9	5.6
Gestational Age	≥37 weeks (Term)	24	14.6
(n 164)	≥32 weeks < 37 weeks (Late Pre-term)	78	47.6
	<32 weeks (Very and Extreme Pre-term)	62	37.8
Place of birth	Inborn (within ESUTH)	92	55.8
(n 165)	Out-born (outside ESUTH)	73	44.2
**ANC attended	Yes	141	88.1
(n 160)	No	19	11.9
Mode of Delivery		100	60.6
(n 165)	Operative	65	39.4
	Appropriate size for GA	97	64.2
(n 151)	Small for GA (Includes IUGR, AGA and SGA)	54	35.8
Duration of hospital stay (days) (n 109)	1-7	47	43.2
	8-14 days	25	22.9
	≥ 14		

*ESUTH: Enugu State University Teaching Hospital
**ANC: Antenatal Care

We also identified a number of co-morbidities among the participants, as summarized in Table 2. Majority of the babies developed Asphyxia (78.8%) and recurrent Apnoea (68.4%) during admission and about two-thirds required a form of respiratory support at one time or the other. Fewer proportion of the babies were exposed to Malaria in pregnancy (27.5%), or subsequently developed Necrotizing Enterocolitis (10.4%) and Anaemia (21.3%) while on admission. Close to half (45.2%) also developed septicaemia, while nearly one-in-five had Neonatal Jaundice. Episodes of recurrent hypoglycaemia were not common, having been observed in just over 17% of the participants, unlike hypothermia, which was recorded in nearly 54%.

Table 2: Co-morbidities diagnosed in preterm infants seen at ESUTH during study period

Morbidities	Parameter	Number %	Outcome		P-value
			Survived	Died	
Asphyxia (n 146)	Yes	28 (19)	17 (61)	11 (39)	0.324
	No	118 (81)	83 (70)	35 (30)	
Respiratory support¶[1] (n 153)	Yes	96 (63)	53 (54)	44 (46)	0.001*
	No	57 (37)	52 (91)	5 (9)	
Recurrent apnea (n 148)	Yes	48 (32)	12 (25)	36 (75)	0.001*
	No	100 (68)	88 (88)	12 (12)	
Anemia ± Blood transfusion (n 141)	Yes	30 (21)	20 (67)	10 (33)	0.926
	No	111 (79)	75 (68)	36 (32)	
Neonatal Malaria (n 129)	Yes	34 (26)	30 (88)	4 (12)	0.001*
	No	95 (74)	55 (58)	40 (42)	
Neonatal sepsis (n 137)	Yes	61 (46)	41 (67)	20 (33)	0.989
	No	76 (54)	51 (68)	25 (32)	
Necrotizing Enterocolitis (n 127)	Yes	16 (13)	12 (75)	4 (25)	0.505
	No	111 (87)	74 (67)	37 (33)	
Neonatal Jaundice± EBT¶[2] (n 117)	Yes	24 (20)	17 (71)	7 (29)	0.561
	No	93 (80)	60 (65)	33 (35)	
Congenital Malformation¶[3] (n 121)	Yes	6 (5)	4 (66)	2 (34)	0.536**
	No	115 (95)	75 (65)	40 (35)	
Recurrent Hypoglycemia (n 142)	Yes	28 (20)	19 (68)	9 (32)	0.975
	No	114 (80)	77 (67)	37 (33)	
Recurrent Hypothermia (n 141)	Yes	75 (53)	47 (63)	28 (37)	0.283
	No	66 (47)	47 (71)	19 (29)	

* P statistically significant
**Yates correction applied
¶[1] Including one or more of Oxygen, CPAP, Surfactant, Caffeine Citrate and Aminophylline
¶[2] EBT: Exchange Blood Transfusion and Phototherapy
¶[3] Includes Down syndrome, Patent Ductus Arteriosus and Hydrocephalus

The final results of a multi-stage Binary Logistic Regression (Table 3) to determine the predictors of survival in these neonates showed that birth at <32 weeks of gestational age is associated with an 88% less chance of survival (OR 0.17; CI 0.03-0.50; P<0.01), while recurrent episodes of Apnoea are associated with a 93% less chance of survival (OR 0.07; CI 0.02-0.34; P<0.01). We also observed that neonates who were exposed to malaria in-utero were about 15 times more likely to survive than those not exposed to such (OR 15.41; CI 2.22-106.91; P=0.01). Although need for respiratory support is associated with 72% less chance of survival, this did not attain statistical significance.

Finally, we observed that there was no significant association between survival in these group of babies and maternal pre-natal attendances to ANC, mode of delivery and birth weight. So also, neonatal morbidities like NEC, hypothermia, hypoglycaemia, septicaemia, anaemia or NNJ have no significant association with survival of the LBW infants in our study (Table 3).

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Table 3: Steps 1 and 2 Binary Logistics Regression

Support variables	Independent variables	Step 1 OR (95% Cl)	Significance *P-value*	Step 2 OR (95% Cl)	Significance *-value*
ANC in Pregnancy	Attended (vs. Not)	4.53 (1.63, 12.62)	0.004*	1.53 (0.25, 9.57)	0.650
Mode of delivery	Spontaneous (vs. Operative)	0.38 (0.15, 0.80)	0.010*	0.53 (0.13, 2.17)	0.380
Gestational Age	[illegible]	0.11 (0.05, 0.24)	0.000*	0.12 (0.03, 0.50)	0.004*
Respiratory Support	Needed (vs. Not needed)	0.07 (0.02, 0.23)	0.000*	0.28 (0.05, 1.68)	0.160
Recurrent Apnoea	Developed (vs. Not)	0.05 (0.02, 0.11)	0.000*	0.07 (0.02, 0.34)	0.001*
Malaria	Developed (vs. Not)	5.46 (1.78, 16.72)	0.003*	15.41 (2.22, 106.91)	0.010*
Birth Weight	≥ 1.5kg (vs. < 1.5kg)	0.18 (0.38, 0.83)	0.000*	0.93 (0.18, 4.73)	0.930

- *Statistically significant
- Only results of Step 2 Analysis were accepted as final
- Odd ratio (OR) and 95% Confidence Interval (CI)
- Only statistically significant results from Step 1 were shown
- Responses in parentheses represent the reference responses.
- All results are shown to 2 decimal places, except where p is < 0.00, in which case it is shown to 3 decimal places

DISCUSSION

The low birth weight babies in this study had male preponderance. This is at variance with the established pattern of female predominance observed from other studies, probably due to differences in methodology (Onyiriuka, 2010; Zeleke et al. 2012; Mumbare et al. 2012, Chukwudi et al. 2002). Female gender predominance amongst low birth weight newborns is attributable to the greater lean body mass and less body fat seen in male newborns than in females, possibly due to the effects of fetal testosterone production (Milner, 1996). Approximately 86% of the LBWs in the present study were preterm births; a finding which is also in contrast with the reports that IUGR is common among LBW deliveries in developing countries while in the developed countries, the predominant cause of LBW is preterm birth. (Mavalankar et al. 1992; Villar and Belizán, 1982; Ndu et al. 2014; Kliegman, 1996). This reversal may be due to the introduction of assisted reproductive technologies and increased multiple conception rates in developing countries (Umeora et al. 2011).

Predictors of survival in LBW newborns are important because they indicate where resources should be directed during newborn care and assist clinical decision making. This study revealed that birth at <32 weeks of gestational age and recurrent episodes of apnoea were significantly associated with decreased likelihood of survival. These associations are not surprising and similar to the findings of other LBW survival studies (Basu et al, 2008). Interestingly, it was also noted that neonates who were exposed to malaria in-utero were about 15 times more likely to survive than those not exposed. The reason for this finding is not immediately clear. However, a Cochrane review on antenatal corticosteroids for women at risk for preterm birth showed that treatment with a single course of antenatal corticosteroids decreased the risk of neonatal death by 31% (Roberts and Dalziel, 2006). Similarly, other studies have shown that antenatal administration of steroids to women at risk of preterm birth is a predictor of increased survival (Sabine et al. 2014; Onyiriuka, 2010) The high level of cortisol associated with metabolic stress induced by plasmodium malaria parasitemia (Esan et al. 2014), may also explain the greater survival rate of LBW neonates with congenital malaria noted in this study.

A systematic review by Medlock et al of existing research in prediction of mortality in very preterm infants reported that seven input variables were frequently found to predict improved survival in multivariate models

(Medlock et al. 2011). They concluded that multivariate models generally predict mortality better than birth weight or gestational age alone.

CONCLUSION

We conclude that, for low birth weight neonates in a low resource setting, births at less than 32 weeks of completed gestation and recurrent episodes of apnoea are significantly associated with less chances of survival, while intra-uterine exposure to malaria confers a higher chance of survival. We also found no significant associations between survival and neonatal co-morbidities like necrotizing enterocolitis, hypothermia, hypoglycaemia, septicaemia, anaemia and NNJ, or with birth weight, mode of delivery and maternal pre-natal attendances to ante-natal care.

LIMITATIONS

Some of the mothers interviewed could not remember their Last Menstrual Period and we had to use the New Ballard Score to estimate their baby gestational age at birth. Such scoring systems are subject to observational errors and accuracy after 48 hours of life is affected. Similarly, APGAR scoring for diagnosis asphyxia was not feasible especially for babies delivered outside the study center especially by traditional birth attendants who are not familiar with the scoring system. In such cases we resorted to history at birth which is subject to recall bias.

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AUTHORS CONTRIBUTIONS

Research idea was conceived by EU and AIN. The Introduction and methodology was drafted by EU and ODIC. Data analysis, result section and abstract done by COI with contribution from ODIC. NIK wrote the discussion with inputs from all the authors. All authors contributed in drafting the questionnaire, data collection and review of final manuscript.

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